Review Article

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AN OVERVIEW ON OSTEOCLAST REGULATION DURING ORTHODONTIC TOOTH MOVEMENT

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ABSTRACT

Conventional orthodontics result in formation of compression zone and tension zone on either side of periodontal ligament. Osteoclast responsible for bone resorption appears on the compression side while bone forming osteoblast appears on tension side with the resultant tooth movement being dependent on osteoblast-osteoclast interaction. During the orthodontic tooth movement, in the initial phase a hyalinization zone appears that impedes the tooth movement unless removed by osteoclast. Thus the faster the osteoclast are recruited to the compression side the faster the tooth movement thus highlighting the importance of recruitment of osteoclast .Therefore this review intends to focus on the regulation of osteoclast during orthodontic tooth movement.

KEYWORDS: Compression zone; pressure zone; hyalinization zone; osteoclast; orthodontic tooth movement

INTRODUCTION

Conventional orthodontics is also known as PDL-mediated orthodontics[1] as the tooth movement relies on the remodeling of both alveolar bone and periodontal ligament. When mechanical stimuli in the form of orthodontic force is applied to the periodontium two distinct regions can be identified on either sides of the PDL namely pressure side where the PDL is compressed and the tension side where the PDL is stretched.[2,3] Many studies focusing on the biology of tooth movement have evidenced that osteoclast appear in the pressure side and osteoblast on the tension side facilitating tooth movement.In this context, orthodontic tooth movement (OTM) is said to be dependent on osteoblastic and osteoclastic periodontal remodeling. Apart from osteoblast and osteoclast, osteocytes, osteoprogenitor and bone lining cells play a significant role during OTM.[4] The OTM is characterized by 3 phases *(Burstone 1962)*, initial phase where in rapid tooth movement occurs following orthodontic force,a lag phase with no tooth movement produced by hyalinization of PDL in the pressure side and a post lag phase with restablishment of tooth movement. Hyalinisation during the lag phase denotes an area of necrosis and so no tooth movement occurs until this impeding tissue is removed by osteoclasts.[1,5] Taking into consideration of this fact, it can be logically assumed that the faster the osteoclast are recruited to the compression side the faster the clearance of hyalinised zone with resultant increase in the tooth movement.[6] This review focuses on recruitment and regulation of osteoclast during OTM .

Recruitment Of Osteoclast During Orthodontic Tooth Movement

The bone resorbing osteoclast cell is normally differentiated from the hematopoietic stem cells (HSC). For the osteoclast generation the HSC enters the monocytic differentiation pathway and gives rise to the granulocyte/macrophage colony forming unit (GM-CFU) which can differentiate into G-CFU or M-CFU. M-CFU under the presence of M-CSF (macrophage colony stimulating factor) differentiates to monocytes and these mononuclear osteoclast precursors further differentiate forming preosteoclast which ultimately fuse to form multinucleated

osteoclast.[7] There are 3 distinct phases in the lifecycle of an osteoclast namely proliferative phase within bone marrow (4-5 days), migratory phase via blood stream (5-13days) and resorptive phase witnessing active multinucleated osteoclast resorbing bone (10-11days). Thus for osteoclastogenesis to occur osteoclast precursors should be recruited to the site of bone resorption that is the compression side of PDL.[8] But the origin of osteoclast precursors in response to orthodontic loading is still a subject of controversy.[9] According to a study done by Rody *et al*., (2001) on the recruitment of osteoclast in OTM the precursors of these osteoclast can be traced to be coming from the alveolar bone marrow than from the local PDL cells.[6] Study done by T. PeterTsay *et al*., demonstrated that initially the osteoclast arise from precursors in the periodontal membrane which later are substituted by those originating from the bone marrow.[10] In a study on the recruitment of osteoclast during experimental tooth movement in young and adult rats, Yijin Ren *et al*., observed that osteoclast recruitment is faster in young rats.[2] Osteoclast differentiation and activation are governed by two important factors M-CSF and RANKL.[1,11] RANKL which is expressed on surface of osteoblast and bone marrow stromal cells belongs to the TNF superfamily while its receptor RANK is located on surface of osteoclast precursor.[3,12] M-CSF is conducive to the survival, proliferation and differentiation of early osteoclast precursors.[11] The receptor for M-CSF (macrophage colony stimulating factor) identified as c-Fms is expressed on the early stage osteoclast precursors whereas RANK is expressed in late stage precursors.[9] During OTM, much of alveolar remodeling relies on RANK-RANKL interaction. Normally, in the absence of compressive force, osteoclastogenesis is inhibited by the OPG (Osteoprotegrin), produced by osteoblast, that acts to inhibit this RANK-RANKL interaction. Thus OPG is a negative regulator for orthodontic tooth movement and this has been proved in a study conducted by OShiro *et al*.[12] When orthodontic force is applied this inhibitory mechanism is suspended resulting in increased release of RANKL (receptor activator of NF-κB) by PDL cells thereby creating a favourable environment for osteoclast generation.[12,13] Apart from RANK and RANKL there are other molecules that regulate osteoclastogenesis such as arachidonic acid metabolites, chemokines and cytokines.[4,5]

Orthodontic Force Induced Inflammation & Osteoclastogenesis

An acute inflammatory response is set up in the periodontium due to the stretching and compressing of PDL fibres by orthodontic forces releasing inflammatory mediators like prostaglandins (PGE2) and interleukin (IL)-1. Cytokines such as IL-6, TNF-α released during the inflammatory process also influence osteoclastogenesis.[4] PGE2 along with neuropeptides like Substance P, vasointestinal polypeptide (VIP) modulates osteoclastogenesis mainly by intracellular increase of secondary messengers, CAMP and Ca^{2+}, in monocytes capable of activating transcription factor gene within the nucleus.[1,4] Human studies using PGE2 on tooth movement by Yamasaki *et al*., and Anand K Patil *et al*., demonstrated the pivotal role of PGE2 in accelerating tooth movement.[14] TNF-α which is noted to be increased in the compression side of PDL is believed to play a significant role in orthodontically induced tooth movement by stimulating osteoclastic bone resorption.[15] Yet another molecule found to influence differentiation and activation of osteoclast include CC chemokine ligand 2 (CCL2), exerting its effect through its receptor CC chemokine receptor 2 (CCR2) found on surface of osteoclast precursor.[16] Eventually after the osteoclast formation, active osteoclast (polarizes) develops ruffled border and attaches to the bone surface with resultant acidic environment creation for dissolution of bone minerals.[17,18]

Clearance Of Osteoclast During Orthodontic Tooth Movement

The possible mechanism governing clearance of osteoclast from periodontal tissue following orthodontic tooth movement remains ambiguous. A probable explanation for osteoclast clearance would be that these cells after their functional life may experience natural death. Neverthetheless, it is also postulated that the osteoclast may be cleared by programmed cell death otherwise known as apoptosis. Apoptotic cells are characterized by both morphological and biochemical changes like blebbing, presence of apoptotic bodies, fragmentation of DNA (DNA

ladder formation) and above all the process is genetically controlled. A study done by Stephen J. Noxon *et al*., to examine role of osteoclast clearance during tooth movement pointed out to the fact that these osteoclast similar to many other cells are removed atleast in part by apoptosis. The rationale for clearance by apoptosis may be that during orthodontic tooth movement a hypoxic environment is created favouring apoptosis by disrupting normal oxidative pathways, increasing nitric oxide production and inhibiting the apoptosis inhibitor, Bcl-2.Also the Ca2+ concentration increase following bone resorption and the cytokines like TNFα released during the OTM tilt the balance towards osteoclast apoptosis.[17]

CONCLUSION

The regulation of osteoclast is thought of to have a fundamental role during orthodontic tooth movement as the rate of tooth movement is mainly dependent on the removal of the hyalinised zone from the compression side by osteoclast . The osteoclastic regulation is mainly by cell recruitment to and clearance from the pressure zone of PDL.A sound understanding of the biological process behind this regulation can pave way to developments in orthodontic techniques intended to control tooth movement.

CONFLICT OF INTEREST & SOURCE OF FUNDING

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